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EDITORIAL

INTERCHANGE OF INFORMATION

It has been our privilege to visit a number of countries recently, and to have discussions with veterinary surgeons and others on the common problem of health and disease of livestock. Each country has its own special problems which demand separate consideration; at the same time, however, there is much in common in our work throughout the world. Our essential task is so to control disease and maintain and improve health in livestock that not only will individual countries gain but that the whole world will be better supplied with the products of the animals concerned. There never has been an occasion when it was more necessary to exert all our efforts to increase the production of such products, and therefore to put into operation methods of control which have been proved of value.

As we have pointed out in previous issues of the Journal, all countries have not been equally fortunate in being able to continue during recent years their research work into the causes and the evolving of methods of control of the diseases which give rise to relatively heavy losses. In some countries, also, conditions have been such that infectious diseases have increased in incidence with consequent economic losses. We in this country have been able to continue and to extend very considerably our work in these directions, with the result that we have a clearer conception of the handling of some disease conditions than in the past. This applies also to some other countries. The veterinary profession is the body which must accept responsibility for advising on disease problems and for the operating of control measures decided upon. It is very necessary, therefore, that all available knowledge should be at the disposal of veterinarians throughout the world, and that means should be adopted whereby it is possible to disseminate the findings of workers, both those who carry out the necessary researches and those who have experience of field methods of control.

There are several ways in which this can be accomplished. Visits by experienced workers to other countries is one method, and, provided that sufficient time can be spent in these countries, good results will follow in general.

This has been shown to occur, but time is necessary, and it is not always convenient or possible for a worker to undertake lengthy visits to other countries. Another scheme is to receive veterinarians and other scientific personnel from countries into the laboratories where the work is in progress, and to give them facilities not only to see and discuss the work in progress but to participate in it. The experience and training acquired by such visitors enables them to judge in how far the methods worked out in other countries can be applied to problems in their own country, and to put into operation identical or modified schemes. This method has already yielded results of value, and should be encouraged. A third method is the convening of conferences or congresses at which veterinarians from many countries foregather and exchange views, experiences and ideas. The great benefit to be derived from such meetings is the mass of information which can be acquired in a short space of time, for a number of workers on a single subject or on one aspect of a subject get together, discuss their experiences, and often come to a definite conclusion on the most convenient and economic way of applying their results. Further, at such meetings it is possible for an individual to select a laboratory or institution, represented by the workers present, from which more information can be obtained. During the war and in the immediate post-war period we have missed these conferences. The time is opportune now, however, to revive them, and it is definitely encouraging to see that the various instructional congresses are again being held. It is good to renew acquaintance with workers we have known in the past and to meet the younger generation which is springing up in the veterinary field throughout the world. There are several such conferences of importance to the veterinary profession, and it is good to see that we are well represented at them. The meeting which appeals to the greatest number of veterinarians, however, is the International Veterinary Congress, and it is very gratifying that it has been found possible to organise the next meeting so soon after the end of the war. It is to be hoped that all countries will be well represented at the forthcoming International Veterinary Congress, which is to be held in London from August 8 to 13 this year. There is much to discuss, and all countries will benefit from the deliberations.

GENERAL ARTICLES

FUNCTIONAL INFERTILITY IN CATTLE, WITH REFERENCE TO ENDOCRINE THERAPY

By J. G. WILSON, M.R.C.V.S.

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THE average stock owner thinks that every bovine mating should result in conception. Actually this state of affairs is often very closely approached in *beef cattle* which live an almost natural life at free range and are encouraged to "breed for fertility" by the rapid culling from the herd of any infertile cows. For example, I have known of a beef bull which put 60 cows in calf within the year with 61 matings, and similar results are by no means rare.

In *dairy cattle,* however, with their more unnatural life, heavy lactation and often deficient nutrition, the general conception rate is not nearly so good.

The published results of the artificial insemination centres in the South West indicate an average conception rate to first service of about 60 per cent and the results of natural mating probably have a similar average.

My experiences show that most of this infertility is of a temporary nature and will yield to time and treatment.

In the South West this temporary infertility appears to have two main causes:

(1) Infective disease of the genital tract, both specific and non-specific.
(2) Functional derangement, as suggested by the history and clinical examination.

I propose to deal with the various types of functional trouble found in this second class, with remarks on their treatment with endocrine products now available.

But first, a few remarks on the clinical diagnosis of these cases.

History.—In the *individual* case in an otherwise fertile herd the main points are whether or not the cow is coming into œstrus and, if so, whether the cycles are regular or irregular.

Sometimes a whole herd appears affected with the same type of functional infertility, suggesting a common cause.

Our only other clinical aid to diagnosis at the moment is the examination and manipulation of the uterus and ovaries "per rectum," when follicles, corpora lutea and cysts (if any) can be easily palpated and expressed or ruptured if considered necessary.

No *biological tests* have so far been elaborated in the cow as an aid to diagnosis. Asdell[1] postulates a very low threshold for sex hormones in the cow and in his "Patterns of Mammalian Reproduction" puts man at the top of the threshold list and the cow at the bottom—incidentally, it takes only

0.25 mgm. of stilbœstrol dipropionate to induce œstrus in the ovariectomised heifer.[1]

Types of Functional Infertility in the Cow

(1) *Anœstrus.*—When a cow is not observed to be coming into season at all, two conditions of the ovaries are found on rectal examination:

(a) Very small inactive ovaries indicating "*dead anœstrus.*" The rational endocrine treatment for this condition is *pregnant mare's serum,* of which 1,500 units are recommended, injected intravenously, but as there is some danger of anaphylactic shock if the dose has to be repeated, I have mainly used 3,000 units intramuscularly; this usually has to be repeated. The results of my work with P.M.S. in the South West have been disappointing and the use of 25-35 mg. stilbœstrol dipropionate appears to produce equally good effects in this condition.

One veterinary practitioner has told me that anœstrus cows which will not respond to stilbœstrol respond to œstradiol, and vice versa.

With many cases of anœstrus, especially in heifers in winter, we have to wait until early summer when the grass has had its effect, or "flushing" with protein in autumn may yield successful results.

(b) In other cases of "anœstrus" the ovaries are found to be normal in size with a corpus luteum present in one of them. Two separate conditions are found:

(i) *Sub-œstrus* in which repeated examinations show the cow to be "cycling" but not exhibiting "mating behaviour" with other cows.

(ii) The corpus luteum may be *persistent*; they are often deeply embedded in the ovary and may be cystic.

If the corpus luteum cannot be expressed by rectal manipulation, a large dose of stilbœstrol may cause it to regress and the cow to come into season.

Incidentally, quite large doses of stilbœstrol usually fail to induce œstrus when the anœstrus is due to well-established pregnancy.

I would like to mention that stilbœstrol dipropionate properly used is the cheapest and most useful endocrine product in veterinary practice.

Other successful uses for this product are:

(a) Expulsion of a mummified fœtus.

(b) Expulsion of the contents of closed pyometra.

(c) Clearing up of purulent or catarrhal endometritis, *before* the cow comes into season after calving. However, if used in *cycling cows* or in too large doses in the above conditions it may produce cystic ovaries with nymphomania.

(2) *Cystic Ovaries.*—I wish to consider only those associated with nymphomania as the others may be of different and varied œtiology. The cysts may be large, up to the size of an orange, or small, suggesting persistent mature follicles. They are more commonly of the large type and easily ruptured "per rectum"; some respond to a single rupturing, but they usually re-form.

Good results are reported from America following 10,000 units of chorionic gonadotrophin (from human pregnancy urine).

Hancock[2] treated 12 cows with 800-3,200 units of chorionic gonadotrophin intravenously. Normal cycles were restored after a single injection in eight cases, including five which were exhibiting nymphomania; two responded to two doses and seven cows became pregnant with a total of eleven matings, after further injections of the hormone.

I have had successful results with 1,000-2,500 units, intramuscularly; the nymphomania disappearing with resumption of normal cycles in nearly all cases, but further treatment was usually necessary to ensure pregnancy.

(3) *Habitual Abortion.*—The abortions, usually in individual cows, are apparently "physiological" and appear unassociated with infective disease. I include the phenomenon of mummified fœtus in this category as it is often repeated in the same cow.

The abortions occur usually between the third and fourth months of pregnancy, about the time when the placenta is taking over the production of the hormones that maintain pregnancy.

Gould[3] has had results with the implantation of 50 mg. of progesterone. I should have thought this dose should be higher, say 500 mg.

I have had apparent results in one or two cases with 1,000 units of chorionic gonadotrophin at the time of mating to ensure formation of an adequate corpus luteum.

(4) *Ovarian Dysfunction.*—I have given this name to a condition found most frequently in Channel Island cattle; it often affects a whole herd or a large proportion of it at the same time; but occasionally may be found in the individual cow.

It appears to be a temporary condition consisting of a period of delayed fertility. It seems to be functional in nature and can sometimes be associated with environmental defects such as unfavourable weather, malnutrition and soil mineral imbalances.

Rectal findings are not constant and include very small functional ovaries (resembling those of an anœstrus animal just beginning to respond to P.M.S.), delayed ovulation, failure of ovulation, formation of atypical corpora lutea and sometimes the only finding is one ovary small and non-functional, although theoretically this should not interfere with conception.

Cycles are often irregular, usually a few days longer than the normal three weeks, or they may occur at intervals of multiples of three weeks, i.e., with periods of anœstrus or sub-œstrus intervening.

The endocrine deficiency has appeared to me to be on the luteal side, and I have had apparently good results in several outbreaks with chorionic gonadotrophin in doses of 500-1,000 units injected at the time of mating.

Results are difficult to assess as the condition is usually of such a temporary nature. Often this condition is found in animals with a high milk yield, so possibly the recent discovery of the effects of the lactogenic hormone of the pituitary gland on the function of the corpus luteum may shed some light on this problem.

Types of Functional Infertility in the Bull

(1) *Anaphrodisia.*—Lack of desire and "slowness," usually with no relationship to the quality of semen produced.

In some cases the cause may be *psychological,* an inhibition to the sexual reflexes having been set up by some painful or frightening experience at service. Change of environment of mating often effects a cure.

In other cases over-use and a lowered output of the male hormone are probably the most common causes.

I have tried P.M.S. in a number of cases, but the improvement, if any, is usually only temporary.

I believe that luteinising hormone has been used with success in some cases; theoretically, it should stimulate the interstitial cells of the testes to produce more testosterone.

Possibly testosterone itself may be of use; we do not know the dose for the bull and overdosing would probably do more harm than good.

(2) *Poor Quality Semen.*—P.M.S. is supposed to stimulate the seminiferous tubules. I have had disappointing results following its use in old bulls, but on occasion apparent success has been found in young bulls. The results may possibly have been due to improvements in nutrition and environment carried out at the same time.

I have not tried luteinising hormone in these cases, but hope to try *testosterone* combined with fructose estimation as an indication of the testosterone level.

To sum up, from an agriculturalist's point of view, I consider that with the possible exception of some of the special uses of stilbœstrol, sex endocrine therapy in cattle, in our present state of knowledge, is neither an economic proposition nor good husbandry, as the individual cow with persistent functional trouble would be best culled from the herd, as the trouble may well be hereditary and the herd functional infertility such as anœstrus and ovarian dysfunction would probably be best tackled and prevented from the environmental and nutritional angle.

But, as the present-day emphasis is on the salvage of as many breeding cows as possible and as the veterinary practitioner must try something while he waits for nature to adjust herself to the strains and stresses inflicted on the long-suffering dairy cow, the demand for hormones will go on.

However, the treatment of some of these conditions with endocrines coupled with careful clinical observations of the results may help to increase our knowledge of *reproductive physiology* and so help the research worker to furnish us with bigger and better hormones.

REFERENCES

(1) Asdell: "Patterns of Mammalian Reproduction."
(2) Hancock, J. L.: *Vet. Rec., 59,* 639-641.
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CAUSES OF STERILITY IN BULLS IN SOUTHERN ENGLAND

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Continued.

CASE HISTORIES OF STERILE BULLS

(wherever a reproductive organ is not mentioned it was normal)

1. (AB 6, Testicular Degeneration)

History.—Guernsey, 8 years old, well-bred bull. Was first put to service when one year old. Previous owner sold him as defective. Fertility rate was 50 per cent (one service each) for healthy cows and 35 per cent (five services each) for the whole herd. Daily ration comprised dairy concentrates 3 lb., greens 20 lb. and hay 35 lb. or more. Received no exercise. Previous service six days before examination.

Behaviour at service.—" 3," cow not in heat.

Clinical examination.—Testicles three-fourths the normal size and turgid, with their long axis directed obliquely from in front backwards and downwards.

Advice.—A course of 6 weekly injections (first, second and third 750 units each, fourth, fifth and sixth 1,500 units each) of PMS with sexual rest. Daily ration to consist of concentrates of 8 lb., silage 10 lb. and hay 20 lb., with regular exercise for 45 minutes every day. Cows to be served in the middle or towards the end of heat.

Subsequent observations.—After treatment his behaviour improved to " 1 " (occasionally " 2 "). Semen showed improvement in density, motility and longevity, but the percentage of abnormal sperm remained unchanged. Owner was advised to use him and report. A few months later he was reported working satisfactorily. He was examined once again a year later. His fertility rate during the year had risen to 75 per cent (one service each) for healthy cows and 45 per cent (two services each) for the whole herd. Behaviour and semen were similar to those after treatment, except for a decline in sperm numbers and reduction in the percentage of abnormal sperm. Since the bull was nearing old age, owner was advised to reinforce his vitality with PMS every breeding season and avoid using him more than once a week.

2. (AB 8, Testicular Degeneration)

History.—Guernsey, 3 years old, well-bred bull. Was first put to service when 11 months old. After working for six months with a fertility rate of 40 per cent, became progressively slow at service and ultimately was unable to jump. A course of 3,000 units of PMS failed to effect improvement. Daily ration comprised dairy concentrates 3 lb. (in breeding season only) and as much hay as he could eat. Was turned out for grazing daily. Previous service 4 months before examination.

Behaviour at service.—" 4 " - " 7," one ordinary cow and one in heat. Presence of cow invoked sexual response only after he had been walked away

from her a few times; this procedure failed after the first jump. Penile rigidity subnormal, with difficulty in insertion. Refractory period after ejaculation entailed prolonged depression.

Clinical examination.—Testicles three-fourths the normal size. Epididymal tails small and soft. Testicles often kept in tucked-up position, giving the ventral part of scrotum the appearance of a wrinkled sac of skin. Intra-abdominal part of vas deferens thick but not sensitive.

Advice.—A course of 3 weekly injections (2,000 units each) of PMS, with sexual rest. Daily ration as for AB 6.

Subsequent observations.—After treatment behaviour improved to "3," penile rigidity and semen showed improvement in all respects. Owner described change in the position of testicles: not held so high as before. The bull was used, and re-examined 4 months later. Behaviour changed to "1" and penile rigidity and semen quality showed further improvement. Though insertion was satisfactory, he had difficulty in reaching cow's vagina. Digging a shallow pit for the cow to stand in during service, standing the bull on a raised platform or allowing him service on inclined ground did not help. A further course of 3 weekly injections (1,500 units each) of PMS was tried. This improved the erectile power of penis but difficulty in reaching the vagina could not be overcome completely. At this stage his fertility rate was a little over 60 per cent. As owner was keen to have as many calves from this bull as possible, it was advised to collect and use his semen artificially, as there was no difficulty in collection by artificial vagina. This procedure met success; his fertility rate is 100 per cent.

3. (AB 9, Testicular Degeneration)

History.—Shorthorn, 3 years old, well-bred bull. Was purchased at the age of 2 years. During the year preceding examination his fertility rate was 45-50 per cent. Daily ration comprised a mixture of oats and dairy concentrates 15 lb. and a handful or two of hay. Received very little exercise. Previous service 8 days before examination.

Behaviour at service.—"2," cow not in heat.

Clinical examination.—Abnormal fat deposition around spermatic cord and in proximal part of scrotum.

Advice.—A course of 6 injections (2 grams each) of ascorbic acid at four days' interval with sexual rest. Daily ration of concentrates to be reduced to 6 lb. silage and hay as for AB 6. Vigorous exercise for 45 minutes daily.

Subsequent observations.—After treatment behaviour improved to "1" and semen showed improvement in density, motility and longevity. Increase to 61.1 per cent in fertility rate reported by owner after 3 months' use. Is still under observation.

4. (AB 11, Testicular Degeneration)

History.—Shorthorn, 5 years old. Was first put to service when 11 months old. Fertility rate during 6 months after purchase (at 3 years) was 70 per cent,

but it gradually declined to zero in the following 9 months. In the 9 months preceding examination he served 20 cows without success. Daily ration comprised No. 1 N.C.F. cake and oats 3½ lb., a mixture of sugar-beet pulp, diced mangolds, swedes and treacle 6 lb. and good meadow hay in sufficient quantity. Was turned out with heifers for one month every summer, remaining 11 months being spent in the loose-box with no exercise.

Behaviour at service.—" 4," cow not in heat. Penile rigidity subnormal but no difficulty in insertion. Copulatory movements uninterested and slow: three preceding each ejaculate.

Clinical examination.—Testicles three-fourths the normal size and turgid.

Advice.—Nil, bull was going for slaughter.

Autopsy.—Testicles small as stated above. Sections showed from 70 per cent (right) to 90 per cent (left) tubules in a state of degeneration, with vacuolisation of epithelial sheet in many parts. Spermatogenic cells had broken down and accumulated in tubular lumina. In addition to changes characterising hydropic degeneration, in many parts the pyknotic nuclei of spermatogenic cells had atrophied (one-fifth to one-half the normal size) and appeared as bold hyperchromatic granules. This change was much more pronounced in left than in right testicle. In some tubules there was evidence of sperm production but their numbers were very small, while in others, spermatogenesis had not progressed beyond spermatocytes or spermatids.

5. (AB 12, Testicular Degeneration)

History.—Shorthorn, 3½ years old. Was first put to service when 11 months old. Fertility rate declined from 100 per cent to 25 per cent during the year preceding examination. Was used as a communal sire. Daily ration comprised swedes, mangolds and hay, as much as he could eat. Was tethered outside every summer, but spent winter months tied up in a small box (where he could hardly stand) with no exercise. Previous service 14 days before examination.

Behaviour at service.—" 3," cow not in heat. After insertion into artificial vagina he paused for 5 seconds and did not ejaculate until third stroke every time. This was not noticed when he served a cow.

Clinical examination.—Testicles three-fourths the normal size and kept in tucked-up position.

Advice.—Retesting after four weeks.

Subsequent observations.—Nil; efforts to contact owner failed.

6. (AB 14, Testicular Degeneration)

History.—Ayrshire, 1½ years old. Started serving cows when 9 months old, possibly earlier. During 6 months prior to examination he served one heifer and three cows without success. Daily ration comprised dairy concentrates 9 lb., mangolds 12 lb. and hay, as much as he could eat. Ration in the previous winter was concentrates 18 lb., mangolds 24 lb. and hay *ad lib.* Received 20 minutes' exercise twice weekly. Day of previous service not known.

Behaviour at service.—" 1," cow not in heat. After mounting, could not

take out penis until two or three strokes inside prepuce. This happened in 3 out of 7 jumps. Penile rigidity subnormal.

Clinical examination.—Long axis of testicles inclined from behind forwards and downwards. Right epididymal head enlarged.

Advice.—A course of PMS with sexual rest. High-grade fish-meal to replace one-tenth of concentrates. Regular exercise for one hour daily. Cows to be served twice in each heat (he had very few animals to breed).

Subsequent observations.—Nil, bull sold after one injection of PMS without intimation.

7. (AB 15, Testicular Degeneration)

History.—Shorthorn, 4 years old. Was first put to service when 15 months old. Produced a few calves, fertility rate being 20 per cent. Daily ration comprised linseed cake 2 lb., oats 3 lb., mangolds 10 lb. and hay 20 lb. Addition of fish-meal to ration for 4 months did not improve fertility. Was tethered outside regularly. Previous service 5 days before examination.

Behaviour at service.—" 1," cow in heat.

Clinical examination.—Testicles three-fifths the normal size and turgid. Seminal vesicles sensitive to palpation but of normal size.

Advice.—Nil, bull was going for slaughter.

Autopsy.—Testicles small, as stated before. Sections showed a severe breakdown of spermatids and spermatocytes; cells of Sertoli and spermatogenic appeared undamaged. Tubular lumina were hardly discernible, as they were full of multi-nucleated cells and cytoplasmic masses of various sizes. The latter were globular or irregular in outline and eosinophilic in staining character, and showed a marked tendency to coalesce and form larger masses. Sperm production was seen only in one-third to one-half of the seminiferous tubules and their numbers were very small. Inter-tubular spaces showed a certain amount of fibrosis in some parts: being more pronounced in right than in left testicle. Distance between two adjacent tubules across the fibrosed area in right testicle was increased to 245 μ in some places.

8. (AB 16, Testicular Degeneration)

History.—Guernsey, 3 years old. Was first put to service when 1 year old. Fertility rate of 75 per cent (one to three services) shown in first year declined to 25 per cent (one to four services) in the second year of service. Conception rate to first service only was half of these figures, i.e. 37.5 per cent and 12.0 per cent, respectively. Daily ration comprised dairy concentrates 10 lb., kale 30 lb., and enough hay (concentrates only allowed for 6 months in the year). Was tethered on pasture in summer but no arrangements made for exercise in winter. Previous service 4 days before examination.

Behaviour at service.—" 4," cow not in heat. After mounting, stroked inside prepuce twice before penis came out. This was not noticed on subsequent jumps.

Clinical examination.—Testicles turgid.

Advice.—Retesting after 6 weeks' rest. Concentrates to be fed throughout the year after replacing them up to 10 per cent with blood-meal. Cows to be served twice in each heat (in view of a poor quality of semen in the first ejaculate).

Subsequent observations.—Nil, efforts to contact owner failed.

9. (AB 17, Testicular Degeneration)

History.—Guernsey, 3 years old. Was purchased at the age of 2 years. Before that he was used 4-5 times every other day for a long period; records of services and fertility were not available. Fertility rate during the second year of service was 24 per cent. Feeding and management as for AB 16. Previous service 7 days before examination.

Behaviour at service.—" 4," cow not in heat. Penile rigidity subnormal. Insertion preceded vulvar titilation at every service.

Clinical examination.—Normal.

Advice.—Administration of thyroprotein for a month with sexual rest. Feeding as for AB 16.

Subsequent observations.—As for AB 16.

10. (AB 20, Testicular Degeneration)

History.—Fresian, 2 years old. Was purchased at the age of 16 months. Served 20 cows one to three times in each heat for 6 months without success. Daily ration comprised dairy cake 4 lb., greens and peas (with kale in winter) 20 lb. and enough hay. Received no exercise except moving about in an enclosure, 40 x 40 yards, with concrete floor and no inducement to move about. Previous service 15 days before examination.

Behaviour at service.—" 4," cow in heat.

Clinical examination.—Testicles soft and flabby. Left epididymal tail soft in texture and prominent.

Advice.—A course of ascorbic acid, shark-liver oil in ration on alternate days and sexual rest for 6 weeks. Concentrates to be increased to 7 lb. and greens reduced to 10 lb.

Subsequent observations.—Instructions not followed, bull sent for slaughter without intimation.

11. (AB 21, Testicular Degeneration)

History.—Fresian, 9 years old, well-bred, proven bull. Was purchased at the age of 8½ years. During 6 months preceding examination showed a fertility rate of 30-58 per cent, with ejaculates selected on the basis of good motility for artificial insemination. A short time ago showed low sperm count: 396,000 per c.mm. Daily ration comprised concentrates (bean-meal, fish-meal, oats and linseed) 6 lb. and sufficient good meadow hay, with greens whenever available. Was slowly walked for half an hour daily as exercise. Previous service 12 days before examination.

Behaviour at service.—" 2," cow not in heat.

Clinical examination.—Testicles and epididymal tails soft, the latter being smaller in size as well. Spermatic cord very long, testicles hanging like a pendulum about 16 inches above the ground plane. Seminal vesicles harder than normal. Abdomen abnormally large.

Advice.—A course of PMS with sexual rest for 6 weeks. Concentrates to be increased to 12 lb. and hay reduced to 20 lb., with vigorous exercise for one hour daily.

Subsequent observations.—Instructions not followed but was rested for 6 months. Re-examination showed improvement in behaviour to "1." Semen improved in density, motility and longevity. Percentage of abnormal sperm reduced but still above normal. As he is awaiting experimental treatment, effects of semen improvement in terms of actual conceptions could not be ascertained.

12. (AB 23, Testicular Degeneration)

History.—Shorthorn, 2 years old, well-bred bull. Was purchased at the age of 1 year and 10 months with history of pneumonia resulting from a fall in river at the age of 1 year and 4 months. In 2 months preceding examination showed a fertility rate of 17 per cent (only 1 of the 6 cows served was in-calf). Grazed on pasture daily and occasionally received a handful or two of hay. Previous service 1 week before examination.

Behaviour at service.—"2," cow not in heat. Gave a few strokes inside prepuce before penis came out; this was not noticed in subsequent jumps.

Clinical examination.—Testicles soft and flabby. Left epididymal head nodulated laterally. Stiffness and indifferent action of lumbar region and lameness of right hind leg like AB 3.

Advice.—Retesting after a course of ascorbic acid and shark liver oil in food. Massage with a stimulating liniment over lumbar and hip joints. Ration to be corrected as for AB 6.

Subsequent observations.—Instructions not followed, bull sent for slaughter without intimation.

13. (AB 26, Testicular Degeneration)

History.—Fresian, 5 years old. Was purchased at the age of 3 years. Fertility rate declined from 65 per cent in fourth to 29 per cent in fifth year of life. Daily ration comprised cake 2 lb., grains 2 lb., kale 20 lb., and hay as much as he could eat. Regularly grazed with the herd. Previous service 4 months before examination.

Behaviour at service.—"6," cow not in heat. Refused two cows but served the third at a different place.

Clinical examination.—Testicles three-fourths the normal size, left one being soft. Occasionally seen masturbating. Abdomen abnormally large.

Advice.—A course of PMS with sexual rest. Daily ration to consist of concentrates 8 lb., silage (preferably roots) 10 lb., and hay not more than 15 lb.

Subsequent observations.—Instructions not followed, bull sent for slaughter without intimation.

14. (AB 27, Testicular Degeneration)

History.—Ayrshire, 2 years old. Was first put to service when 1 year old. Fertility rate in first year of service was 20 per cent. Semen was reported to be of poor motility. No one knew how the bull was fed or exercised; both seemed at fault. Previous service 6 weeks before examination.

Behaviour at service.—" 1," cow not in heat.

Clinical examination.—Testicles soft and flabby.

Advice.—A course of 6 injections (2 grams each) of ascorbic acid at four days' interval with sexual rest. Daily ration and exercise as for AB 6.

Subsequent observations.—After treatment semen improved in density, motility and longevity. Was tried on 4 cows, 2 of which became pregnant. To reinforce vitality a course of PMS was recommended. Is still under observation.

15. (AB 28, Testicular Degeneration)

History.—Shorthorn, $3\frac{1}{2}$ years old, well-bred bull. Was first put to service when 10 months old. Fertility rate declined from normal to 21 per cent (three to four services each time) in the 6 months preceding examination. Daily ration comprised palm kernel cake 4 lb., grain mixture (oats 3 parts, barley 1 part, and peas 1 part) 6 lb., swedes and kale 10-15 lb., and sufficient good quality hay. Received light exercise daily. Previous service 15 days before examination.

Behaviour at service.—" 1," cow not in heat. Refused to ejaculate into artificial vagina after first collection.

Clinical examination.—Testicles three-fourths the normal size, soft and kept in tucked-in position like AB 12. Spermatic cord short.

Advice.—A course of PMS with the addition of blood-meal to ration.

Subsequent observations.—Instructions not followed, bull sent for slaughter without intimation.

16. (AB 31, Testicular Degeneration)

History.—Shorthorn, $2\frac{1}{4}$ years old, well-bred bull. Was purchased at the stage of $1\frac{3}{4}$ years. Was reported to give usually immotile and sometimes reasonably motile sperm. Fertility rate with ejaculates selected on the basis of good motility was 70 per cent during 6 months preceding examination. Daily ration comprised concentrates (oats 2 parts, calf-nuts 3 parts, linseed-cake 1 part and meat-meal 1 part) 8 lb., and seeds hay *ad lib.*, with outside grazing whenever possible. Previous service 11 days before examination.

Behaviour at service.—" 1," cow not in heat. Glans erected a few seconds later than hinder parts of penis. Penile rigidity subnormal.

Clinical examination.—Testicles two-thirds the normal size (left smaller than right), soft and flabby and often kept in tucked-up position. Spermatic cord short. On walking, both legs showed lameness like AB 3.

Advice.—A course of 6 injections (2 grams each) of ascorbic acid at four days' interval and 500,000 units of vitamin A once a week for 6 weeks with sexual rest.

Subsequent observations.—After treatment semen improved in density, motility, longevity, and, to some extent, morphology. This improvement was of a very temporary nature and vanished in a week. Two weeks later he commenced ejaculating practically dead sperm again, density being very low. Testicles became softer still and more flabby. In the meantime his semen having been found grossly infected with staphylococci (no such evidence of infection was seen on bacteriological examination carried out on 6 ejaculates procured on two different occasions in this laboratory), he was withdrawn from service.

17. (AB 32, Testicular Degeneration)

History.—Jersey, 4½ years old, well-bred bull. Was purchased at the age of 4 years. About 95 per cent of semen samples were reported to be dead; of the remaining 5 per cent those showing good motility gave 60 per cent fertility rate during 6 months preceding examination. Ration and exercise as for AB 31. Previous service 1 month before examination.

Behaviour at service.—" 2," cow not in heat.

Clinical examination.—Testicles slightly soft. Seminal vesicles enlarged but not sensitive. Abdomen large.

Advice.—A course of 6 weekly injections (1,500 units each) of PMS with sexual rest. Daily ration of hay not to exceed 20 lb., with regular brisk exercise.

Subsequent observations.—After treatment, behaviour improved to " 1." Semen showed improvement in density, motility and longevity, but a rise in sperm abnormalities. Improvement being maintained at four subsequent collections at 4 days' interval, semen was used for artificial insemination. For 50 cows so inseminated in 8 weeks, fertility rate rose to 85 per cent. Is still under observation and is being considered for a further course of PMS or ascorbic acid.

To be continued.

AN INVESTIGATION INTO A DISEASE OF HOUND WHELPS

By R. W. L. CHESNEY
Porlock

Introduction

EARLY in 1947 I was called in to treat an illness occurring in very young hound whelps. It was a recurrence of a similar condition which had fatal results in the two preceding years, but the losses were now much higher. Characteristic symptoms were weakness in the hind legs and/or sudden death within the first three to four weeks of life.

History

Prior to 1945, the mortality in young pups was considered to be within the normal range, that is, one or two in every litter, but in 1945 the rate suddenly increased considerably. No investigation was undertaken and no statistics are available. In 1946 the mortality was even greater, but still no serious attempt was made to find the cause. Losses in 1947 were very heavy and the symptoms in the sick puppies were identical with those of the preceding years. The mortality rate was approximately 80 per cent. There had been an attempt to increase the number of hounds and so more bitches had been mated than in the preceding years. Of the 20 bitches mated, only 10 conceived, and of those 10 only five reared any live pups. The only bitch to rear a healthy litter did so away from the kennels, and so it was thought best to allow all the 1948 bitches to whelp away, but the first two to do so in 1948 needed treatment for their pups and so the rest of the bitches whelped at the kennels. The mortality rate for 1948 was 16 per cent. Fifteen bitches had been mated, seven conceived and six reared live pups.

Symptoms

These can be divided into two main types:

(1) Illness starting within a few days of birth. The whelp becoming dull and listless, off its food, has a staring coat and sometimes a little yellowish coloured diarrhœa. The temperature varies between 102 and 103 degrees, and although it returns to normal after the pup is treated with penicillin or one of the sulphonamides, this does not have any influence on the course of the disease and the pup dies before it is a week old. Occasionally a whelp will be found dead two to three days after birth and there have been no symptoms of illness.

(2) The majority of whelps were apparently quite fit for the first week or two of life and then, with very few exceptions, would react in one of the following ways:

(a) Drop dead without warning and often just after a meal.

(b) Commence to lose condition fairly rapidly, bowel motions semi-liquid and yellow in colour, coats lose lustre, the abdomen becomes " tucked-

up" and there is a "tied-in" appearance over the loins. There is a gradual progressive paraplegia and a week or two after onset of symptoms the pup may be walking on its front legs and carrying its hind legs off the ground. The appetites remain unimpaired, temperatures normal, and the pups appear bright-eyed and fairly happy. Some may have fits. The illness lasts from one to three weeks and death occurs suddenly. An odd whelp in a litter might not show any symptoms and would grow up normally.

At no time throughout the period of illness in the pups was there any illness in the bitches and there was never any suggestion of the pups not receiving sufficient nourishment.

A characteristic feature of the illness in the pups was the presence of ulcers between the main pad and the outer or inner pad on the fore and/or hind feet. These ulcers started as small sores, about the size of a pin's head, and were noticed within a day or two of birth. If the pup was not treated with sulphamezathine and the period of illness was longer than one week, then the sores became ulcers of approximately $\frac{1}{4}$ in. diameter, which penetrated the skin and exposed the underlying tendons. Under treatment with SMZ (the sulphamezathine) the sores disappeared within a few days.

Post-mortem Examinations

1947: The first examination this year was made on one of "Passion's" puppies. Lab. A reported beta-hæmolytic streptococci (BHS) and worms.

Other examinations of dead pups from the same litter were carried out by me and revealed ulcers on the pads, hæmorrhage or blood clot in the pericardial sac, slight patchy thickening of the bowel wall, a few coccidia, and worms.

The last pup of this litter was deteriorating in condition and was sent alive to Lab. B, where it was destroyed, and a post-mortem examination revealed a salmonella and B. coli in the bowel, but no BHS. Cultures from all the organs were sterile. B. coli injected into mice showed only a mild pathogenicity.

I carried out examinations on three dead puppies from "Makeshift's" litter and the pictures were identical with those in "Passion's" pups.

1948: One dead pup out of "Passion's" litter was sent to Lab. B, which reported a heavy infestation with coccidia.

Two pups from "Active's" litter were examined by me and the pictures were identical with last year's pups of "Passion" and "Makeshift," and there was a heavy coccidial content.

Diagnosis and Treatment

1947: The earliest attempts at control of the disease involved the use of penicillin and sulphonamides, but these had no influence on the illness. Lab. A reported the presence of beta-hæmolytic streptococci in a vaginal swab and in a dead puppy, and advised vaccination of the bitches and the pups,

together with adequate worming of the pups with "Nema" capsules. This was carried out in nine bitches prior to whelping; in five bitches after whelping and also in their whelps. This did not affect the onset or course of the disease and puppies died in a similar manner to those with four bitches which had not been vaccinated.

A very small sample of fæces from one of the affected pups was sent to Lab. A, which reported roundworms.

Vaginal swabs from six bitches were then sent to Lab. B and the report was B. coli in all of them.

Sulphamezathine (SMZ), which had been used in one litter of ailing pups, produced an amazing recovery. This was followed 10 days later by a relapse, and SMZ again helped in a temporary recovery. This was the same litter in which BHS had been diagnosed and they had been vaccinated with BHS vaccine. Lab. A had stated that SMZ was of no use in the treatment of BHS infections unless there was a febrile temperature. In none of the sick pups was there more than a degree or two rise in temperature. The sole survivor in this litter was again relapsing and so it was sent alive to Lab. B, where it was destroyed. No trace of BHS could be found in the carcase and there were no organisms in any of the tissues, but a salmonella and B. coli were isolated from the contents of the bowel. The B. coli were injected into mice, and some of the mice were treated with SMZ and remained resistant.

Vaginal swabs from 12 bitches were then sent to Lab. B, which reported B. coli in eight, BHS in one, staphylococci in two, and B. coli and non-hæmolytic streptococci in one. This latter swab was one of two taken at the same time from the same bitch. The other swab was sent to Lab. A, which reported BHS.

Forty-five puppies died from this disease in 1947 and 11 survived.

Blood samples taken from the puppies which had survived showed no evidence of distemper antibody.

Was the disease caused by BHS, B. coli or some other factor?

Laboratory findings were at variance. Vaccination with BHS had been carried out, but it had not helped. Mice had been protected against the B. coli by the use of SMZ and this drug had been of use in the treatment of the pups. Therefore the causal factor in the disease was susceptible to SMZ. This drug is said to be of particular value in the treatment of infection due to gram-negative organisms and is highly active against coccidia. As there had been no suggestion of coccidia from either laboratory it was thought probable that B. coli was the cause of the disease as it was such a common finding and was susceptible to SMZ. It was decided that as the whelping season for 1947 had finished, all the bitches which were to be mated in 1948 should receive a course of autogenous B. coli vaccine early in pregnancy, and should there be any illness in the puppies they would receive SMZ.

1948: The B. coli vaccination was carried out in four bitches soon after mating, and three bitches were left unvaccinated as controls. "Passion" was

the first bitch to whelp and she had been vaccinated. A month earlier Lab. A had reported finding hookworm and coccidia in this bitch's fæces. On the fourth day of life, two of her four pups were found to be sluggish and they died on the seventh day. Unfortunately, I was not informed of this. At one month another puppy was taken ill and demonstrated symptoms identical with those seen in 1947. It died after a few days and the carcase was sent to Lab. B, which reported a heavy infestation with coccidia as the cause of death. A sample of fæces from "Passion" was sent to Lab. B and they found a moderate number of hookworm eggs but no coccidia. (Compare this with the report from Lab. A two months ago.)

The remaining puppy was unthrifty and showed a slight weakness in the hind legs. I examined a sample of its fæces and found a heavy content of hookworm and a moderate number of coccidia. It was wormed and then put on to SMZ, and made a rapid recovery and remained well. The bitch was also treated with SMZ and three weeks later an examination of the pup's fæces showed only a moderate hookworm content and an absence of coccidia. Four months later the bitch's fæces were examined at Lab. C, which reported moderate hookworm and an absence of coccidia.

In the case of "Passion," the vaccination of the bitch had not influenced the disease in the pups, but SMZ was effective in curing the ailing puppy. Were we dealing with B. coli or coccidia? Samples of fæces from bitches which had been mated were sent for examination and the results showed all of them to be heavily infested with hookworm and about three-quarters had a variable content of coccidia.

The possible causative factors had now increased to four, namely, beta-hæmolytic streptococci, B. coli, hookworm and coccidia. In an attempt to clarify the position, vaginal swabs were taken from seven of the bitches which had whelped in 1947 and/or 1948. Two swabs were inserted at the same time into each bitch and one swab was sent to Lab. A and the other to Lab. B. The results were as follows:

	Lab. A	*Lab. B*
Gadfly	BHS, B. coli, etc.	BHS
Merlin	BHS, B. coli, etc.	B. coli
Pansy	BHS, B. coli, etc.	BHS, B. coli
Possible	BHS	Cocci
Active	BHS	BHS, B. coli
Dabchick	Sterile	BHS, B. coli
Passion	BHS	BHS

(It will be noted that both of Passion's swabs were negative for B. coli.)

There is little difference to be found in these two reports apart from the comment made by the laboratories. Lab. A states that BHS is the important organism and B. coli a contaminant; whereas Lab. B considers both organisms capable of being normal inhabitants of the vaginal flora.

In 1947 the bitches and pups were vaccinated with an autogenous BHS vaccine, and this did not influence the mortality rate. In 1948 the bitches were vaccinated with an autogenous B. coli vaccine, and this made no difference to the onset or course of the disease.

SMZ is stated to be of no value in the treatment of BHS, but was proved effective against B. coli in experiments in mice. But with the first 1948 bitch to whelp, where the pups died from coccidiosis and SMZ saved the last pup, the two swabs from the bitch both showed BHS only. These findings lead to the conclusion that coccidiosis was the probable cause of the illness.

As there was never any serious rise in temperature in the sick pups and their appetites remained unimpaired, it was considered that the loss of condition, weight and use of the hind legs was secondary to a bowel disorder, especially as coccidia and hookworm eggs had been found in the fæces.

Further experiments were carried out to determine which organism was responsible.

The bitch " Possible," which showed hookworm only in the fæces, was not treated with SMZ and neither were her puppies, and they remained well in spite of the presence of BHS in the mother's vagina and the fact that they had not been vaccinated.

Owing to the great need of the kennels to save as many pups as possible, it was not considered policy to adopt the same procedure with the bitches showing coccidia in the fæces. These received a course of SMZ one week before whelping and their pups when one week old. In two of these litters (Cosy and Active), one or two pups were kept as controls, and it was found that they did not suffer from the disease. This was attributed to the fact that the bitch had been treated. (It will be remembered that " Passion," which was infected with coccidia, had not been treated prior to whelping and her pups became infected and the untreated ones died from coccidiosis.)

A study of the case sheet of " Active " reveals that she was infected with coccidia, but was not treated until three days after whelping, and her pups were not treated until they were a week old. Two pups died when seven days old, i.e. untreated, and the post-mortem examination revealed coccidia. The other pups thrived normally. This case emphasises the importance of treating the bitch prior to whelping in order to reduce the number of organisms voided, and which might be ingested by the puppies when they are suckling.

It would appear that we have arrived at coccidia as the causal organism. But are we correct in assuming that the very presence of coccidia is sufficient to set up illness? If we examine the whelping history of " Merlin," we will find that our assumption is incorrect. Vaginal swabs from this bitch revealed BHS and B. coli. Examination of fæces showed the presence of moderate to slight hookworm content and a negligible number of coccidia. No vaccines or SMZ were given and she whelped four healthy puppies, and these, in turn, received no SMZ. Forty-eight days after whelping another sample of fæces from the bitch showed only slight hookworm but heavy coccidial content. Four

days later a sample of fæces from the puppies was examined, and although there were numerous coccidial oocysts, there was an absence of hookworm eggs. The puppies were perfectly healthy and their fæces were normal in appearance. In this first puppy fæcal examination there was also recorded a medium-heavy toxocara infestation, and the pups were therefore wormed with Cooper's liquid medicine, which contains in every drachm 1 mgm. arecoline and two-thirds minim of oil of chenopodium. A week later a further sample of fæces from the pups was examined at Lab. C, and the result was as follows: Coccidial oocysts still present but in much reduced numbers; the ascarid eggs have disappeared, but a very few hookworm eggs are now present. Incidentally, the puppies had been away from the bitch for about a week when their first fæcal examination was made. It would appear, then, that the presence of a variable number of coccidia is not in itself sufficient to set up illness. What, then, is the predisposing factor whereby an animal succumbs to coccidiosis?

We have found that vaccination with BHS and B. coli had no influence on the disease. In the case of "Merlin," which was infected with these organisms and was not vaccinated, no illness occurred in the puppies. If these two organisms are ruled out, we have only roundworms and hookworms as suspicious factors. The presence of roundworms in "Merlin's" pups certainly had no exciting nature associated with them. This brings us to hookworms. It is well known that these can set up disease in puppies, but none of the cardinal symptoms of that disease have been demonstrated, and, as far as is known, the hookworm is not susceptible to SMZ. But in the case of "Merlin" and her pups, the hookworm content was lower than in the other hounds. Might not the hookworm be the predisposing factor?

PASSION (CASE SHEET)

1946: Half the litter died early, but no symptoms recorded.

1947: May 5. BHS stock vaccine.

„ 9. „ „ „

„ 24. Whelped 9 puppies.
Vaginal swab sent to Lab. A revealed BHS.

„ 25. Bitch and 9 pups inoculated BHS stock v.

„ 27. „ „ 9 „ „ „ „ „
1 pup died; no post-mortem.

„ 30. „ „ 8 „ inoculated with BHS stock v.
1 pup died; no post-mortem.
All pups had sores on feet between main pad and outer toepad.

June 2. Bitch and 7 pups inoculated with BHS stock v.

„ 3. 1 pup died; no post-mortem.

„ 5. „ „ 6 „ inoculated with BHS stock v.

June 5-16. Bitch and 6 puppies appeared to thrive and then one pup died and the carcase was sent to Lab. A The report was BHS and worms. The pups were wormed with "Nema."

„ 19. Another pup died but no post-mortem made.

„ 24. „ „ „ . I carried out a post-mortem examination and this revealed: ulcers on pads, a number of worms in the bowel and a fair number of coccidia; the pericardial sac was dilated with blood clot, but there was no congestion of blood vessels or extravasation into the musculature or serous membranes.

„ 24-28. During this time the three remaining pups were deteriorating in condition; there was a loss of s/c fat, a weakness in the hind quarters and a "tied-in" appearance over the loins. They were wormed again. There were no abnormal temperatures.

„ 28-30. The pups lost the use of the hind legs. They were quite happy and hungry.

„ 30. A very small sample of fæces was sent to Lab. A, which reported worm eggs.

July 1. The pups only were put on to SMZ for seven days (0.25 gm. b.i.d.).

„ 5. An amazing improvement. The pups were almost normal in their gait, but the bodily "tucked-in" condition remained.

„ 9. Three pups wormed, with result.

„ 11. Three pups standing well on legs, fairly bright and active, twice the size of ten days ago but still very tucked-in and lacking in s/c fat. Put on to vitamin B.

„ 13. No change.

„ 15. Slight deterioration in strength of legs. They were put on to PHTHZ (0.25 gm. b.i.d.). [phthalylsulphathiazole.]

„ 18. Definite deterioration. All very weak on hind legs and during movement most of the weight is taken on the front legs, and sometimes, when they attempt to run, the hind legs are carried in the air for a few steps. They are still fairly happy and eating well. No abnormal temperatures. One pup has had a fit.

„ 19. One pup that had a fit died suddenly and the carcase decomposed rapidly. No post-mortem. The other two sick pups were put back on to SMZ (0.25 gm. b.i.d.).

„ 22. Definite improvement. Stronger on legs, more active and coats silkier.

„ 25. Both well and vigorous.

July 29. Vaginal swab from bitch sent to Lab. B and the result was B. coli. Both pups well.

„ 31. One pup having fits so it was chloroformed and sent with the live pup to Lab. B.

Aug. 4. The live pup deteriorated rapidly at the laboratory and was destroyed on the fourth day. The post-mortem examination revealed a mild enteritis, but no worms. Cultures from all organs were sterile, but a salmonella and B. coli were obtained from the intestines. There was no trace of BHS. Mice were injected with the B. coli to test for pathogenicity, and this proved to be mild in nature. Tissue from the pup was injected into ferrets, and two out of three developed distemper, but the laboratory stated that this should not be considered as conclusive proof.
The dead pup which had been sent to the laboratory was decomposed on arrival.

„ 22. Vaginal swab from "Passion" sent to Lab. B and B. coli was isolated.

1948: Jan./Feb. Eight injections of autogenous B. coli vaccine. Sample of fæces from "Passion" sent to Lab. A, which reported coccidia and hookworm.

Mar. 15. Whelped 13 pups, of which nine were destroyed on the first day. On the fourth day of life, two pups were found to be sluggish and they died when they were a week old. No post-mortem examination was made.

April 13. The two remaining pups had an unhealthy appearance and were below weight for their age, were lacking in subcutaneous fat, had ulcers on the hind feet, and one pup was only half the size of the other.

„ 14. The small pup very ill.

„ 15. „ „ „ died and the organs and pads sent to Lab. B.

„ 19. Sample of fæces from "Passion" sent to Lab. B, which reported worm eggs but no coccidia.
The other pup was wormed. It was slightly tucked-in over the loins and showed weakness in the hind legs.

„ 21. Lab. B report on the dead pup showed a heavy infestation with coccidia. Tissue had been injected into ferrets to check for distemper.

„ 22. "Passion" and the pup were put on to SMZ. The pup was definitely suffering from the same illness which occurred in the 1947 litter. Its fæces showed hookworm and coccidia.

„ 28. Puppy showing great improvement.

May 2. Puppy appeared quite normal in its gait and its bodily condition was improving.

„ 5. Puppy quite normal and the ulcers on the feet have healed.

May 12. Puppy's fæces examined and were negative.
„ 22. Puppy perfectly fit and sent out "to walk."
Sept. Vaginal swab from "Passion" sent to:
Lab. A, which reported BHS.
Lab. B, „ „ BHS.
„ Fæces from "Passion" sent to Lab. C, which reported hookworm eggs but no coccidia.
Report on ferret/distemper test (see April 21) was negative.

"COSY" (CASE SHEET)

1946: All pups died early. Some died suddenly without symptoms, others developed leg weakness prior to death.
1947: Whelped seven pups; six died before one month and showed similar symptoms to last year. The survivor, "Ringdove," did not show any symptoms and is healthy.
Vaginal swab from "Cosy" examined at Lab. B revealed B. coli.
1948: *This bitch was not inoculated with B. coli vaccine.* Fæces were positive for hookworm and coccidia at Labs. A and B.
July 1. The bitch was treated with sulphamezathine.
„ 8. „ „ whelped five puppies.
„ 15. Three pups were put on to SMZ and two were kept as controls.
„ 19. One control pup died from intussusception and the organs were sent to Lab. B, and the report was negative (special care having been taken to search for coccidia and spirochætes).
Oct. The three treated and the surviving control puppies have not shown a day's illness.

"ACTIVE" (CASE SHEET)

(Born 1943 and was the only survivor in the litter)

1946: Half the litter died from illness but the symptoms were not recorded.
1947: Whelped six pups which died before they were one month. Symptoms were mainly leg weakness.
Vaginal swab from "Active" examined at Lab. B revealed hæmolytic streptococci.
1948: *Not injected with B. coli.*
April 10. Fæces from bitch were examined at Lab. B and showed very heavy infestation with coccidia.
„ 13. Whelped eight pups.
„ 16. Bitch treated with SMZ.
„ 19. Two pups died and bowel contained coccidia. (All the puppies showed ulcers on the hind feet between the main pad and the toepads.)
„ 20. Three pups were put on to a sheepdog foster-mother and three were left with "Active." All the pups were given SMZ with the exception of one pup with "Active."

April 21. Fæces from the sheepdog were positive for hookworm but negative for coccidia.

June 19. One puppy died from jaundice.

Sept. All pups very fit and have shown no symptoms of the disease. Fæces from "Active" and puppies sent to Lab. C were positive for hookworm but negative for coccidia.
Vaginal swab from "Active" sent to Lab. A showed BHS.
" " " " sent to Lab. B showed BHS and B. coli.

"GARNET" (CASE SHEET)

1947: May Two injections of BHS stock vaccine.

July 4. Whelped two puppies.

" 5-11. Bitch and pups received two injections BHS autogenous vaccine.

" 11. One pup from "Dora" added to this litter.

" 15-22. Bitch and three pups, three injections BHS autog. v.

" 29. Vaginal swab from "Garnet" sent to Lab. B, which reported B. coli and non-hæm. strep.

Aug. 13. The three pups were deteriorating in condition and they were wormed.

" 15. The pups are still ill and the disease is identical with that shown in "Passion's" pups.

" 16. Fæces from "Garnet" and the puppies were examined by me and they showed hookworm and coccidia. The bitch and pups were put on SMZ.

" 20. Great improvement in the pups.

" 22. Vaginal swabs from "Garnet" sent to Lab. B and the report was B. coli.

" 28. The three pups are quite fit and normal in appearance. Blood from one of "Garnet's" pups and from "Dora's" pup, which was reared with "Garnet," did not contain distemper antibody and failed to neutralise the virus.

"DORA" (CASE SHEET)

1947: May Two injections of BHS stock vaccine.

July 5. Whelped 11 puppies; four were destroyed and one was put with "Garnet."

" 8-22. "Dora" and her six pups received five injections of BHS autogenous vaccine.

" 29. Vaginal swab sent to Lab. B, which reported B. coli.

" 30. Fæces from "Dora" were examined by me and the result was a few hookworm eggs.

Aug. 1. 2 pups injected with 5 c.c. B. coli serum. 2 pups SMZ.
„ 5. 2 „ „ „ „ 2 „
„ 9. 2 „ „ „ „ 2 „
Two pups were kept as controls.
„ 22. All pups are quite fit.
Vaginal swab sent to Lab. B and report B. coli.
Sept. 2. All pups are fit and have been sent out.
Nov. Blood from three of these puppies showed that two of them had no distemper antibody, but the third had. This antibody was probably acquired whilst the puppy was out "at walk."

"VIRGIN" (CASE SHEET)

1947: Whelped six pups, which died within a few days, and the symptoms were not observed.
Aug. Vaginal swab sent to Lab. A showed BHS.
„ „ „ B „ non-HS and B. coli.
1948: Feb. Bitch inoculated with B. coli vaccine.
April Fæces examined at Lab. B were positive for hookworm and coccidia.
„ Bitch treated with SMZ.
May 2. Whelped three weakly pups which were deformed. Although the hind legs were normal, the front legs were abducted from the shoulders at right-angles from the normal position. One pup died from weakness when two days old and the other two were destroyed within a fortnight because there was no change in their condition. They were flat-chested and being unable to use their front legs their only means of locomotion was a pushing action with the hind legs and a slithering on the chest.

(Compare this condition with that found in "Gadfly's puppy.)

"DABCHICK" (CASE SHEET)

1947: May Inoculated with BHS stock vaccine.
June 8. Whelped four pups.
„ 10-24. Bitch and pups received a course of five injections of BHS autogenous vaccine.
July 1. Two pups noticed weak on the hind legs and the other two were slightly affected.
„ 4. Four pups put on to SMZ (0.25 gm. b.i.d. for four days).
„ 8. Four pups improving and are vigorous and happy.
„ 10. Two pups died suddenly. No post-mortem.
„ 11. Other pups showing leg weakness again and put on to vitamin B.
„ 15. One pup weaker and the other stronger than on the 11th. Put on to PHTHZ.

July 18. The weak one now takes most of its weight on the front legs. It is quite happy. Both pups put on to SMZ again.
„ 22. The weak pup now much stronger, walks on all four legs although one leg still weak.
„ 25. The stronger pup sent out "to walk."
„ 31. The weak pup is now quite normal.
Aug. 1. The weak pup died suddenly after drinking its milk. No post-mortem was possible owing to rapid decomposition in the post.
„ 22. Vaginal swab from the bitch sent to Lab. B revealed B. coli. The pup out at walk is quite normal.
1948: Sept. Vaginal swab sent to Lab. A was sterile.
„ „ „ „ B showed BHS.

"MAKESHIFT" (CASE SHEET)

1947: May Two injections BHS stock vaccine.
July 8. Whelped eight puppies; four were destroyed.
„ 11-18. Bitch and four pups received three injections BHS autogenous vaccine.
„ 19. One pup died very suddenly. No post-mortem.
„ 22. One „ „ „ . The post-mortem examination revealed subpericardial hæmorrhage and petechial-hæmorrhages in the small intestine and a thickening of the wall in the large bowel. There were no worms, but hookworm and coccidia were present in moderate amounts.
„ 23. Bitch and two pups, injected with BHS autog. vaccine.
„ 25. One pup died very suddenly. The post-mortem picture was identical with that of the 22nd.
„ 27. The last pup died suddenly and the organs were sent to Lab. B, but were decomposed upon arrival.
None of these pups had shown any symptoms of illness.
„ 29. Vaginal swab from "Makeshift" sent to Lab. B, which reported B. coli.
Aug. 22. Ditto.

"GADFLY" (CASE SHEET)

1948: April Eight injections autogenous B. coli vaccine.
May 14. Fæces sent to Lab. B showed worm eggs but no coccidia. Bitch was put on to SMZ.
„ 27. Whelped three puppies and one died immediately.
June 3. Two pups on to SMZ. One puppy was normal, but the other had been deformed from birth. Its chest was flattened and the forelegs were everted from the shoulder joints and

it could not bring them to the front. Movement was by means of the hind legs.
(Compare this deformity with that found in "Virgin's" puppy.)

„ 15. Both pups quite healthy, but the deformed one was still unable to use its front legs. I decided to experiment with this condition, and, using a three-inch bandage, I brought the front legs into a normal position and bandaged the chest, shoulders and upper portions of the legs.

„ 17. The normal pup had removed the other's bandage a few hours before I arrived and I was amazed to find two puppies walking around the kennel. I could tell which was the affected one because its gait was faulty. Another bandage was affixed, but apparently the other pup soon removed it.

„ 22. Unable to tell which puppy had been deformed. They were both very fit and had shown no symptoms of any illness.

Aug. Both pups quite normal. Sent out "to walk."

Sept. Vaginal swab from "Gadfly" sent to:
Lab. A which reported BHS, staphylococci, B. coli, non-hæm.-strep.
Lab. B. „ „ BHS.

"POSSIBLE" (CASE SHEET)

1948: July Fæces sent to Lab. B and Lab. C showed hookworm but no coccidia.
This bitch was not inoculated with BHS or B. coli vaccine and was not treated with sulphamezathine.

„ 31. Whelped nine pups; five were destroyed.

Aug. 4. Bitch developed metritis as a result of a retained fœtal membrane. Treated with stilbœstrol.

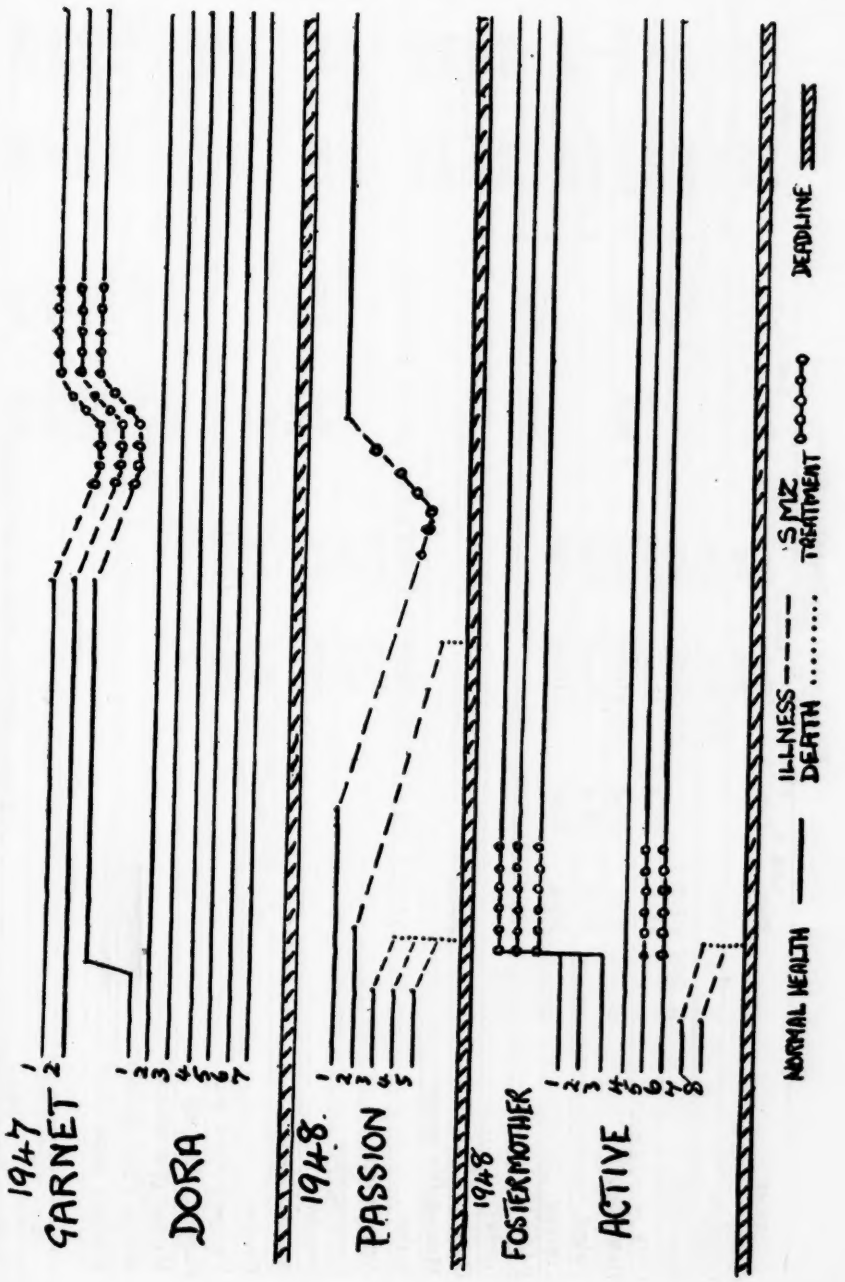
„ 14. Bitch free from vaginal discharge and is improving in condition. The four pups have not shown any sign of illness.

Sept. Fæces from the puppies were sent to Lab. C, which reported toxocara and hookworm.

Vaginal swab from bitch sent to:
Lab. A, which recorded BHS.
Lab. B, „ „ an absence of any organisms.

Puppies remained well.

PUPPIES' AGE IN DAYS
12
24
36
48
60
72
1947
MAKESHIFT
1947
PASSION
1947
COSY
1947
DABCHICK


1947
GARNET
1 2
DORA
1 2 3 4 5 6 7
1948.
PASSION
1 2 3 4 5
1948
FOSTERMOTHER
1 2 3
ACTIVE
4 6 6 7 8
NORMAL HEALTH
ILLNESS
DEATH
SM2
TREATMENT
DEADLINE

Examination of Fæces

NAME	LAB. A Hook.	LAB. A Cocc.	LAB. B Hook.	LAB. B Cocc.	LAB. C Hook.	LAB. C Cocc.	OWN Hook.	OWN Cocc.
Gadfly			Mod.	Neg.			Mod.	Neg.
Virgin			Mod.	Mod.			Mod.	?
Riot			Mod.	Neg.			Mod.	Neg.
Cosy	Mod.	Mod.	Heavy	Slight	Mod.	Neg.	Mod.	?
Dulcet	Mod.	Mod.	Heavy	Slight	Mod.	Neg.	Heavy	Slight
Fidget	Mod.	Mod.	Heavy	Slight			Mod.	?
Coronet	Mod.	Mod.	Heavy	Slight			Mod.	Neg.
Pansy					Mod.	Slight		
Garnet							Mod.	Mod.
Dora							Mod.	Neg.
Makeshift's puppy							Heavy	Mod.
Active			Mod.	Heavy			Mod.	Mod.
Active's pups			Mod.	Heavy				
Fostermother			Mod.	Neg.			Mod.	Neg.
Possible			Slight	Neg.	Mod.	Neg.	Neg.	Neg.
Possible's pups					Mod.	Neg.		
Passion	Mod.	Mod.	Mod.	Neg.				
Passion's dead pup			Neg.	Heavy			Neg.	Mod.
Passion's live pup							Heavy	Mod.
Merlin (1st sample)					Heavy	Slight		
Merlin (2nd sample)					Slight	Heavy		
Merlin's pups (1st)					Neg.	Heavy	Neg.	Mod.
„ „ (2nd)					Slight	Mod.	Neg.	Mod.
„ „ (3rd)					Slight	Mod.	Neg.	Slight
„ „ (4th)					Slight	Mod.	Neg.	Slight

After Treatment with Sulphamezathine

NAME	LAB. A		LAB. B		LAB. C		OWN	
	Hook.	Cocc.	Hook.	Cocc.	Hook.	Cocc.	Hook.	Cocc.
Active					Mod.	Neg.	Neg.	Neg.
Active's pups					Mod.	Neg.	Neg.	Neg.
Passion			Slight	Neg.				
Passion's pup			Slight	Neg.				
Cosy's pup			Neg.	Neg.				

Hook. = Hookworm eggs. Cocc. = Coccidial oocysts (isospora).

SUMMARY OF DIAGNOSES, TREATMENT AND RESULTS

Name 1947	Diagnoses	Treatment	Puppies Untreated	Puppies Treated	Sequel
Active	BHS	—	6	—	No survivors
Virgin	BHS, B. coli	—	6	—	No survivors
Cosy	B. coli	—	7	—	1 survivor
Makeshift	B. coli	BHS		4 BHS	No survivors Coccidia and Hookworm
Dabchick	B. coli, BHS	BHS		4 BHS and SMZ	1 survivor
Passion	B. coli, BHS	BHS		9 BHS and 6 died and then 3 SMZ	No survivors. ? B. coli

ABBREV.—BHS: Beta-hæmolytic streptococci.
SMZ: Sulphamezathine.
NHS: Non-hæmolytic streptococci.

Summary of Diagnoses, Treatments and Results—continued

Name	Diagnosis	Treatment	Puppies Untreated	Puppies Treated	Sequel
Dora	B. coli, Hookworm	BHS	2	2 SMZ 2 B. coli serum	All survived
Garnet	B. coli, NHS, Hookworm, Coccidia	BHS SMZ	—	2 SMZ	Both survived
1948					
Active	BHS, Hookworm, Coccidia	SMZ three days after whelping	3	5 SMZ	Treated pups and control pup survived
Virgin	BHS, B. coli, Hookworm, Coccidia	B. coli SMZ	3	—	Pups deformed destroyed
Cosy	B. coli, Hookworm, Coccidia	SMZ	2	3 SMZ	1 died from intussusception; 4 survived
Passion	BHS, B. coli, Hookworm, Coccidia	B. coli	4	1 SMZ	Treated puppy survived
Gadfly	BHS, Hookworm	B. coli SMZ	—	2 SMZ	Puppies survived
Possible	BHS, Hookworm	—	4	—	Puppies survived
Merlin	BHS, B. Coli Hookworm (slight) Coccidia (heavy)	—	4	—	Puppies survived Coccidia in fæces

"MERLIN" (CASE SHEET)

1948: Sept. 12. Vaginal swab sent to:

Lab. A, which reported BHS, B. coli, staphylococci and non-hæm.-strep.

Lab. B, which reported B. coli.

„ 20. Fæces sent to Lab. C, which reported hookworm and a negligible number of coccidia. No vaccines or SMZ given.

„ 23. Whelped four healthy pups.

Oct. 12. Puppies are very healthy. They have not been treated with SMZ.

„ 20-26. One puppy was noticed quiet and off its food for a few days, but after a dose of castor oil it soon recovered.

Nov. 1. Weaned.

„ 11. Fæces from "Merlin" sent to Lab. C, which reported slight hookworm and heavy coccidial (isospora) infestation.

„ 15. Fæces from puppies sent to Lab. C, which reported negative for hookworm but numerous coccidial oocysts (isospora). Medium-heavy toxocara infestation.

„ 20. Puppies wormed with Cooper's liquid medicine: 60 minims, containing arecoline 1 mgm., ol. chenops 2/3 m., castor oil ad 60 m.

„ 25. Fæces from pups sent to Lab. C:

No toxocara eggs present; very few hookworm eggs; reduced number of coccidial oocysts.

Dec. 14. Fæces from pups sent to Lab. C:

A few toxocara and hookworm eggs; a small number of coccidial oocysts.

„ 29. Fæces from pups sent to Lab. C:

Very small number of toxocara and hookworm eggs; a few coccidial oocysts.

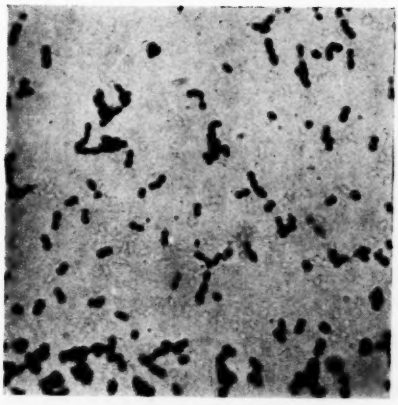
Puppies are in perfect health.

Summary

A disease of very young hound whelps has been described, in which the main symptoms were sudden death without illness at one to three weeks; or death following a few days' illness or a week or two of leg weakness. Post-mortem examinations revealed hæmorrhage into the pericardial sac and/or bowel lesions with or without parasites. Diagnosis was attempted by examina-

tions of: vaginal swabs from suspected bitches; blood samples from recovered puppies; fæces from the bitches and pups; and post-mortem specimens. Organisms isolated were beta-hæmolytic streptococci, Bacterium coli, hookworm and coccidia. Treatment at first was for streptococci with an autogenous vaccine, sulphonamides and penicillin, but this gave no results. As the general symptoms appeared related to the bowel, a trial course of sulphamezathine was administered, and this produced excellent results. Although this drug is usually associated with the treatment of coccidia in other animals, it is not considered satisfactory for that purpose in dogs. Laboratory findings in the early stages of this investigation did not give cause for any suspicion of coccidia as a causal factor in the disease. Experiments carried out with mice inoculated with culture of B. coli from a hound's vagina showed that sulphamezathine was capable of protecting them against an otherwise fatal dose of that organism. This finding, coupled with the good result of the use of the drug in the sick puppies, laid emphasis on the possibility of B. coli as the causal organism and led to the vaccination of the bitches which were to be used for breeding in 1948. An autogenous B. coli vaccine was used and each bitch received eight graduated doses during the early days of pregnancy. The first bitch to whelp lost two puppies in the first week and at one month another pup was showing signs of malnutrition and leg weakness, and it soon died. The sole remaining puppy was also ailing, but after a few days on sulphamezathine it was much better. The post-mortem report on the pup which died showed that it was full of coccidia. A systematic examination was then made of the fæces of all the pregnant bitches, and this showed a heavy infestation with hookworm in every case and a variable number of coccidia in three-quarters of them. It appeared that the B. coli vaccinations had failed to prevent the onset of the disease. Examination of vaginal swabs revealed BHS and B. coli, and as the 1947 vaccinations with BHS and the 1948 vaccinations with B. coli had both failed to stop the disease, it was considered highly probable that these organisms were of secondary importance. The other factors associated with the disease were hookworm and coccidia. Careful observation showed that the presence of hookworm in the bitch's fæces at the time of whelping caused no illness in the puppies; and the same finding was also true for coccidia. Illness occurred when both parasites were present at the same time and, possibly, when the emphasis was on hookworm, although there would have to be a fairly heavy coccidial content. Treatment of a bitch infested with coccidia was usually carried out during the week preceding whelping, and the dose was based on the bodyweight, i.e. 0.05 gm./kilo. twice daily for five days. The puppies were treated during their second week of life and the dose was 0.125 gm. per puppy, twice daily for five days. It was found that when treatment of a bitch was delayed for a few days after whelping, then there was a chance of one or more puppies succumbing to the disease before they were a week old. In some cases where the bitch had been treated the week before whelping, one or two of the puppies were kept without sulphamezathine in order to act as controls. As these pups showed no sign of illness it was thought probable that it might not be necessary to treat the puppies of a litter from a treated bitch.

Photograph 1.



Photograph 2.

Article by Z. Morcos, page 171.

A PSEUDO-TUBERCULOSIS-LIKE DISEASE : Treatment of Mice with Penicillin

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History

Since 1929 three outbreaks occurred among laboratory animals in this department. The first was a virus infection which occurred among guinea-pigs and was investigated by the senior author in 1932. The second was caused by an anærobic organism in rabbits in 1933, and was also investigated by him. The third, which is the outbreak in question, occurred among a group of white mice, 80 in number and of various ages.

The affected mice developed abscesses at various parts of the body, mainly round the face and testicles (photograph I). The infection took rather a chronic course and the affected animals usually died within ten days. The lesions were almost confined to the abscesses, which contained caseous material, thick and cream-like in colour and consistency. Post-mortem did not show gross abnormality in the internal organs.

Ætiology

An organism of the Corynebacterium group was isolated from the heart blood as well as from the lesions of the dead mouse. It is a very small, almost coccus-like bacillus, pleomorphic and gram-positive, taking the stain solidly (photograph II). It grew very poorly on ordinary media; on horse blood agar the colonies were minute, colourless and with no evidence of hæmolysis. Gelatine and coagulated serum were not liquefied. Biochemically, glucose, saccharose, lactose and maltose were fermented with the production of acid only; mannite was *not* attacked; litmus milk was first bleached and coagulated, later becoming acid and the clot partially loosened. Thus the organism isolated does not conform with the classical type of *Corynebacterium pseudotuberculosis ovis,* nor does it conform with *Corynebacterium murisepticum,* which is known to cause septicæmia in mice.

Treatment

Twelve mice with lesions were treated with penicillin subcutaneously without any surgical interference. The first dose was 5,000 units, followed three-hourly by 1,000 units for five successive days, when all the lesions were gradually absorbed and later cleared up. Contacts without apparent lesions were similarly treated, but for three days only, and the outbreak was brought to an end.

Discussion

Organisms of the Corynebacterium group which give rise to suppurative lesions in various animals under normal conditions should be sensitive to penicillin. Records of tests in this direction, however, are very few, probably on account of the difficulty of the *clinical* detection of the disease. To our knowledge, the only available reference is that by Lovell and Cotchin (1947), who studied the effect of penicillin on C. renale *in vitro* and *in vivo*. They found

that of 12 strains tested, sensitivity varied from 0.1 to 0.0001 units per ml. Experiments in mice showed that when penicillin was given early and the doses frequently repeated, treatment was of value, as was judged by cultural tests and histological examination.

Penicillin may, therefore, be recommended with success in suppurative conditions caused by certain members of the Corynebacterium group, as, for example, ovine caseous lymphadenitis and equine ulcerative lymphangitis. It appears to be more reliable than vaccines, which, in whatever manner prepared, have given variable and disappointing results.

Summary

(1) A pseudotuberculosis-like outbreak occurred among a group of white mice.

(2) The causal organism was an unclassified member of the Corynebacterium group, which was described.

(3) Penicillin proved valuable in controlling the outbreak.

REFERENCES

Lovell, R., and Cotchin, E. (1947): *J. Comp. Path.*, 57, 20.
Morcos, Z. (1932): *J. Bact.*, 23, 449.
Morcos, Z. (1933): *J. Bact.*, 25, 239.

NOTICE

A NEW SYRINGE

With the new " Chance " interchangeable all-glass syringe there is no need for the parts to be numbered for identification, for corresponding parts of all syringes of the same capacity rating can be interchanged at will.

If part of this syringe is broken, a new barrel or plunger can be obtained to fit the undamaged part.

The barrel and plunger of this syringe have been made by a new process to extremely fine dimensional limits. The close working clearance between barrel and plunger necessitates extreme care in removing minute particles of dust or other foreign matter before fitting the parts together.

The conditions of the leak test described in British Standard 1263 have been applied in the manufacturing control, and syringes as delivered will comply with this requirement.

Chance interchangeable syringes are made in low-expansion heat-resisting glass, and they can be sterilised by any of the methods described in the Medical Research Council's War Memorandum No. 15. A temperature of 160 deg. C. for one hour is recommended for hot air sterilisation, but there is no risk of damage to the glass in the event of accidental overheating up to 300 deg. C.

The graduations are on the millilitre scale as laid down in British Standard 1263. For practical purposes the ml. and the cc. can be taken as identical; (the ml. is 1/1,000 part of the volume of 1 kg. of pure water at 40 deg. C. and 760 mm. pressure).

A " Record " type needle can be fitted by the use of an adapter.

The sole distributors of this new syringe are Surgical Equipment Supplies, Ltd., Westfields Road, North Acton, London, W.3.